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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/675,208	09/29/2000	Chieko Osumi	195378US0DIV	2452

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EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 04/24/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/675,208

Applicant(s)

OSUMI ET AL.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-16,22-26 and 31-69 is/are pending in the application.
- 4a) Of the above claim(s) 69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-16,22-26 and 31-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on with the application is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledgment

1. The request filed on March 11, 2003 in paper no. 13 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/675208 is acceptable and a RCE has been established. An action on the RCE follows.

2. The amendment filed 3/11/2003 has been entered.

Claims 13-16, 22-26, and 31-69 are pending.

Claims 37-69 have been newly added.

3. Newly submitted claim 69, directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 69 is drawn to a method for producing a polypeptide, which is a separate invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 69 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Claims 13-16, 22-26 and 31-68 are examined in the present office action.

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on April 26, 1996. It is noted, however, that applicant has not filed a certified copy of the Japanese application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 13-16, 22-26 and 31-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 13, "galactinol" is misspelled.

In claim 13, part (1), part (2) and part (4), the word "ability" should be replaced with --polypeptide--. It is unclear how an "ability" can have characteristics associated with it.

In claim 14, the recitation "shown in" should be replaced with --of--. The recitation "shown in" is open language and it is not clear to which bases of SEQ ID NO:1, 2, or 3 Applicant is referring. All subsequent recitations of "shown in" are also rejected.

In claim 15, "galactinol" is misspelled.

In claim 15, line 4, the recitation "1 x" should be replaced with --1X--. All subsequent recitations in which a "x" follows a number are also rejected.

In claim 15, insert the word --molecule-- after the word "DNA".

In claim 23, the words "*Cucurbitaceae Leguminosae* or plant" should be replaced with --*Cucurbitaceae* or *Leguminosae* plant.-- The sentence as written is grammatically incorrect.

In claim 34, the recitation "homology" should be replaced with --sequence identity--. The word "homology" has an evolutionary component that has not been defined. All subsequent recitations of "homology" are also rejected.

In claim 38, "galactinol" is misspelled.

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In claim 38, the recitation "homologous to the coding strand of the coding region" should be deleted. This recitation is superfluous and does not further clarify the scope of the claim.

In claim 44, the words "*Cucurbitaceae Leguminosae* or plant" should be replaced with --*Cucurbitaceae* or *Leguminosae* plant.-- The sentence as written is grammatically incorrect.

In claims 58-67, the second "a" should be replaced with --the--, to make the sentence grammatically correct.

In claim 68, 4th line, the word --sequence-- should be inserted after the word "DNA".

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 13-16, 22-26 and 31-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a DNA sequence or chimeric gene encoding a raffinose synthase having specified biochemical properties, a DNA sequence or chimeric gene comprising a coding region that hybridizes under stringent conditions to the nucleotide sequence of bases 56 to 2407 of SEQ ID NO:4, a DNA sequence or chimeric gene encoding an amino acid sequence of SEQ ID NO:1, 2 or 3, a DNA molecule encoding a raffinose synthase that exhibits an amino acid sequence of

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not less than 35% or 40% of SEQ ID NO:5, or a DNA molecule encoding a raffinose synthase, wherein the DNA molecule exhibits not less than 65% sequence identity to a DNA molecule encoding the amino acids 510 to 610 of SEQ ID NO:5, transformed plant and method for changing the content of raffinose family oligosaccharides in a plant.

The Applicants only disclose a raffinose synthase nucleic acid sequence from cucumber of SEQ ID NO:4 encoding SEQ ID NO:5 (page 60, lines 10-24). The applicants do not identify structural features unique to a raffinose synthase protein that has the specified biochemical properties recited in claim 13, nor the functional domains of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. The claims recite sequences exhibiting at least 35% or 40% sequence identity to sequences encoding SEQ ID NO:5 and sequences that hybridize to SEQ ID NO:4 but Applicants have not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Thus, there is insufficient relevant

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identifying characteristics to allow one skilled in the art to predictably determine such mutants and allelic variants from other plants and organisms, absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

8. Claims 13-16, 22-26 and 31-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim a DNA sequence or chimeric gene encoding a raffinose synthase having specified biochemical properties, a DNA sequence or chimeric gene comprising a coding region that hybridizes under stringent conditions to the nucleotide sequence of bases 56 to 2407 of SEQ ID NO:4, a DNA sequence or chimeric gene encoding an amino acid sequence of SEQ ID NO:1, 2 or 3, a DNA molecule encoding a raffinose synthase that exhibits an amino acid sequence of not less than 35% or 40% of SEQ ID NO:5, or a DNA molecule encoding a raffinose synthase, wherein the DNA molecule exhibits not less than 65% sequence identity to a DNA molecule encoding the amino acids 510 to 610 of SEQ ID NO:5, transformed plant and method for changing the content of raffinose family oligosaccharides in a plant.

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The inventors disclose a nucleic acid sequence of SEQ ID NO: 4 referred to as raffinose synthase and a polypeptide sequence of SEQ ID NO: 5, derived from the former (page 60, lines 10-24). Raffinose synthase catalyzes the formation of raffinose from galactinol and sucrose. The Applicants screened a cDNA library from cucumber and isolated DNA encoding raffinose synthase. The cDNA encoding raffinose synthase was subcloned into a vector in a sense and antisense orientation, operably linked to the 35S promoter. Said constructs were transformed into *Arabidopsis* and subsequent transformed plants were analyzed for raffinose content. In plants harboring either orientation of the isolated raffinose synthase encoding DNA, 0.0 mg/g raffinose were detected compared to wild type whose raffinose content was 0.2 mg/g (page 65, Table 4). The Applicants present three additional sequences SEQ ID NO's : 1, 2, and 3 which are short amino acid sequences taken from SEQ ID NO:5 which they state can be used to generate PCR primers.

The claims are broadly drawn, for example, Applicants claim a nucleic acid molecule encoding a polypeptide, wherein the polypeptide exhibits at least 35% sequence identity to SEQ ID NO:5. The instant specification, however, fails to provide guidance for which amino acids of SEQ ID NO:5 can be altered, substituted or deleted and which amino acids must not be changed, to maintain activity of the encoded protein. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left

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column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65°C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to

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which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe.

Furthermore, the claims are broadly drawn to nucleic acid molecules encoding a plant raffinose synthase that has a homology of not less than 65% in the region between amino acids 510 and 610 of SEQ ID NO:5. However, Peterbauer et al (1999, The Plant Journal 20(5):509-518) teaches a protein exhibiting 72.5% homology which is not a raffinose synthase. Given the lack of guidance in identifying Applicants invention and given the existence of a protein that falls within the scope of the claims that has a wholly different activity, it would require undue experimentation by one skilled in the art to identify a raffinose synthase from the multitude of sequences that fall within the scope of the claims.

Given the unpredictability of determining the function of an isolated nucleic acid that encodes a polypeptide exhibiting as low as 35% sequence identity to SEQ ID NO:5 or a nucleic acid that hybridizes to bases 56 to 2407 of SEQ ID NO:4 for the reasons stated above; given the lack of guidance and working examples of isolating and identifying raffinose synthase genes from the multitude of sequences that would hybridize to bases 56 to 2407 of SEQ ID NO:4 or would encode a protein having at least 35% identity to SEQ ID NO:5, given the state of the prior art which does not provide further guidance about raffinose synthase genes; and given the breadth of the claims which encompass a multitude of sequences that have not been exemplified, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 13-16, 22-26 and 31-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 6166292 (listed in 1449). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are obvious over the claims of Patent No. 6166292. Claims 1-41 are drawn to an isolated DNA which originates from an organism having an ability to produce raffinose from sucrose and galactinol, with the nucleotide sequence comprising at least nucleotide residues 56 to 2407 of the nucleotide sequence of SEQ ID NO:4

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and encodes a protein which has the amino acid sequence of SEQ ID NO:5 exhibiting inherent properties of an isolated raffinose synthase protein as described in Patent No. 6166292 column 3 last paragraph. In addition, claim 25 of the present application which is drawn to an isolated DNA from cucumber that would hybridize under stringent conditions to nucleotides 56-2407 of SEQ ID NO:4 is obvious over Patent No. 6166292 because it is described in said patent the procedure for preparing a DNA encoding a raffinose synthase from cucumber.

11. Claims 13-16, 22-26 and 31-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 8-11, 14, 17, 19-20, and 22-24 of copending Application No. 09/425055. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5, 8-11, 14, 17, 19-20, and 22-24 are drawn to a DNA encoding a raffinose synthase comprising the nucleotide residues 56 to 2407 of SEQ ID NO:4 or a sequence that would hybridize to a nucleic acid molecule comprising nucleotides 56 to 2407 of SEQ ID NO:4, a DNA encoding a protein specified by SEQ ID NO:5, a transformed plant and a method for changing the content of raffinose family oligosaccharides in a plant which reads on the same material as specified in the claims of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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12. Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Heck et al (April, 1993, NCBI Database Accession Number M77475).

The claim is drawn to an isolated DNA molecule that hybridizes to a nucleic acid molecule comprising nucleotide numbers 56 to 2407 of SEQ ID NO:4 and wherein the encoded raffinose synthase has a homology of not less than 65% in the region between amino acids 510 to 610 of SEQ ID NO:6.

Heck et al teach a DNA sequence that would hybridize to Applicants specified sequence and encodes an amino acid sequence that comprises 71.1% sequence identity to the region between amino acids 510 to 610 of SEQ ID NO:5, and as such anticipates the claimed invention.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

April 7, 2003


ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600